REMARKS

Claims 23 to 44 are pending in the application; examiner continues to withdrawn claims 37-44.

Lack of Unity of Invention

Examiner has not responded in the final rejection to the arguments presented by applicant on 11/28/2007 in regard to unity of invention practice. Therefore, the arguments are presented here again for reconsideration by examiner.

Examiner states that the application contains three groups of invention that are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The examiner requested that applicant elect a single invention from the groups I, II and III as defined in the office action - election has been made with traverse.

In examiner's opinion the groups lack a general inventive concept because they lack a special technical feature. The examiner points out that there are **three** inventions, the first being a product and the second and third being methods of producing the product. As pointed out by the examiner, 37 CFR 1.475 provides for a **category for a single product; a single method of making the product, and a single method of using the product.** The examiner then states that inventions II and III are drawn to different methods of MAKING a product and that the methods are different because of the non-overlapping pH conditions.

It is respectfully submitted that the invention III - claims 41-44 - is directed to a method of USING the product of claim 23 and not a method of MAKING the product of claim 23. Note that the product of claim 23 is used as a substrate in the method of claim 41. In other words, claim 41 is directed to USING the metallic object according to claim 23 for immobilizing complementary nucleic acid. Note that in the method step of selecting a pH value and an ion strength the metal oxide layer of the metallic object and the nucleic acid compounds of the coating of the metallic object are referenced. The product of claim 23 is being USED in the claims 41-44 and not MADE by the process of claims 41-44.

Therefore, as a product and a method of using the product pursuant to 37 CFR 1.475(b)(2) **"will be considered to have unity of invention"**, the claims 41-44 must

be rejoined as the special technical feature resides in the product itself.

As regards the special technical feature lacking in the product (invention I) and the method of making the product (invention II), it is respectfully submitted that the prior art *Bitner* does not show STABLE and IRREVERSIBLE INCORPORATION of the terminal ends in the metal oxide layer; incorporation is not shown in *Bitner* - **only sorption** to the substrate surface which is **reversible**. In order to clarify "incorporation" in the metal oxide layer, the claims have been amended to define that a metal oxide layer is grown about the 5'-terminal or 3'-terminal ends and the 5'-terminal or 3'-terminal ends are embedded in the metal oxide layer. Note that incorporation is clearly shown in Fig. 2

The invention II (claims 37-40) are therefore to be rejoined as well.

Rejection under 35 U.S.C. 102

Claims 23-30, 32, 33, 35, 36 stand rejected under 35 U.S.C. 102(b) as being anticipated by *Bitner (EP 0 391 608)*.

The examiner argues that *Bitner* anticipates claim 23 because the reference discloses a solid support comprising an amount of metal oxide with a coating that is comprised of a thin metal oxide layer as disclosed on page 3, line 20; page 4, line 16; page 7, lines 15-16; and nucleic acid molecules having their 5'-terminal or 3'-terminal ends incorporated into the metal oxide layer as disclosed on page 3, lines 22-23.

Examiner in response to arguments section has stated that the presented arguments are not persuasive because the claims set forth "terminal molecule areas" and not "terminal ends".

The claims have been amended to change the language to terminal ends.

Examiner argues that it is inconceivable that not a single one of the nucleic acids in the method of *Bitner* would sorb with their terminal ends to the substrate, especially in view of the statement that hybridization (interaction) is possible for the sorbed nucleic acid of *Bitner*

Applicant would like to stress that nothing is set forth specifically in *Bitner* about the way the nucleic acid is sorbed or which part of the nucleic acid sorbs to the surface The only feature mentioned is that the nucleic acid retains biological accessibility and

reactivity, i.e, hybridization (page 3, lines 21-23). As pointed out before, the hybridization capability has nothing to do with the way the nucleic acid is sorbed to the surface of the metal oxide. It is immaterial whether the 5'-terminal or 3'-terminal ends or the backbone is sorbed. Immobilization of the nucleic acid by way of the backbone is sufficient for enabling hybridization.

As stressed before, *Bitner* discloses that the phosphate groups of the DNA backbone may play a significant role in the sorption of the nucleic acids to the metal oxide (page 5, lines 32-33) so that the disclosure of *Bitner* rather stresses sorption by way of back bone than by 5'-terminal or 3'-terminal ends.

In order to achieve the initial sorption effect according to the present invention the terminal ends are provided with anionic groups such as phosphates, phosphonates or sulfonates (see page 8, 2nd and 3rd full paragraphs, of the specification). The reference *Bitner* does not teach that the DNA should be provided at the terminal ends with such anionic groups in order to effect sorption.

But aside from lack of disclosure as to where sorption occurs or does not occur, the fact remains that *Bitner* fairly discloses only two things:

- DNA sorbs to metal oxide surfaces;
- the backbone is believed to play a significant role in sorption of the nucleic acid to the metal oxide surface.

Based on this disclosure there cannot be anticipation of the subject matter as claimed in claim 23 as follows:

"... wherein the nucleic acid compounds have 5'-terminal or 3'-terminal ends and wherein the 5'-terminal or 3'-terminal ends are **embedded in the metal oxide layer grown about the 5'-terminal or 3'-terminal molecule areas."**

Claim 23 sets forth not only sorption of the nucleic acids to a metallic substrate but also **embedding** in the oxide layer that is **grown about the 5'-terminal or 3'-terminal ends. *Sorption*** is not equivalent to embedding as sorption is a physical process that is reversible. The present invention in claim 23 requires embedding in the metal oxide layer, the metal oxide layer being grown about the terminal ends. *Bitner* does not disclose that metal oxide is being grown about the terminal ends in order to embed the terminal areas in the metal oxide.

Applicant would like to stress that the gist of the invention is that the 5'-terminal or 3'-terminal ends are "incorporated" or, as now more specifically defined in claim 23, are **embedded in the metal oxide layer that is grown about the 5'-terminal or 3'-terminal ends**; see in particular Fig. 2 where embedding in the metal oxide is shown. The 5'-terminal or 3'-terminal ends are not merely **sorbed** to the surface but are **embedded in the grown metal oxide layer** (see page 4, 1st full paragraph, of the specification). The nucleic acids according to the present invention are fixed in the metal oxide and cannot be removed.

The sorbed nucleic acids of *Bitner* however can be desorbed (see page 8, lines 42-46, of *Bitner* where the **desorption** of the nucleic acids is described as an important attribute of the disclosed composition) and there is no teaching in regard to embedding the sorbed portions in a metal oxide layer that is grown about the terminal ends.

The present invention provides a regio-selective incorporation of the nucleic acids by means of the 5'-terminal or 3'-terminal ends and, in this way, the unincorporated sections are freely movable. This makes them accessible for hybridization reactions and also for biological processes in which secondary and tertiary structures of the nucleic acids are important. See particularly page 4, 2nd to 4th full paragraphs, of the instant specification.

Applicant has previously submitted three publications A1, A2, A3 (enclosed in amendment filed 11/28/07) as evidence that the present invention, in addition to maintaining the hybridization capability, also enables the immobilization of the nucleic acid aptamers while maintaining the biological activity; see especially paragraph 2.6. of publication A3 (A1 and A2 describe the inventive method per se). The present invention provides a structural and functional retention that goes far beyond the hybridization capability as evidenced by the functionality of the aptamers fixed on the substrate by means of the method according to the invention (aptamers retain their specificity for binding special cell populations even after immobilization on Ti/Ti alloy; see A3). A3 is proof positive of the regio specificity in regard to immobilization of the nucleic acids achieved with the present invention. Only a freely movable DNA single strand, i.e., not even partially bonded by backbone to the substrate surface, is capable (after immobilization) of forming the defined three-dimensional structure required for realizing

the aptamer functionality.

Claim 23 is therefore neither anticipated nor obvious in view of *Bitner* and should be allowable together with its dependent claims.

Reconsideration and withdrawal of the rejection of the claims under 35 USC 102 are therefore respectfully requested.

Rejection under 35 U.S.C. 103

Claim 31 stands rejected under 35 U.S.C. 103(a) as being unpatentable over *Bitner* in view of *Wengel et al. (US 6,670,461).*

Claim 34 stands rejected under 35 U.S.C. 103(a) as being unpatentable over *Bitner* in view of *Yabusaki et al. (WO 85/02628).*

Claim 23 is believed to be allowable; its dependent claims should be allowable also.

DOUBLE PATENTING REJECTION

Claims 23-26 are rejected on the ground of obviousness-type double patenting over *US 6,524,718.* The instant application is assigned to Technische Universität Dresden, Dresden, Germany. The cited patent was first assigned by the inventors to Merck Patent GmbH, Darmstadt, Germany, and then assigned to Biomet Deutschland GmbH, Berlin, Germany. There is no common ownership. According to MPEP 804 (Heading B. Nonstatutory Double Patenting 1. Obviousness-Type, 1st paragraph):

"Obviousness-type double patenting requires rejection of an application claim when the claimed subject matter is not patentably distinct from the subject **matter claimed in a commonly owned patent, or a non-commonly owned patent but subject to a joint research agreement** as set forth in 35 U.S.C. 103(c)(2) and (3), when the issuance of a second patent would provide unjustified extension of the term of the right to exclude granted by a patent." (Emphasis added.)

There is no common ownership and no joint research agreement. There is no unjustified extension of term of the right to exclude.

Reconsideration and withdrawal of the double patenting rejection of the claims 23-26 are therefore respectfully requested.

CONCLUSION

In view of the foregoing, it is submitted that this application is now in condition for allowance and such allowance is respectfully solicited.

Should the Examiner have any further objections or suggestions, the undersigned would appreciate a phone call or **e-mail** from the examiner to discuss appropriate amendments to place the application into condition for allowance.

Recognizing that Internet communications are not secure, I hereby authorize the USPTO to communicate with me concerning any subject matter of this application by electronic mail. I understand that a copy of these communications will be made of record in the application file.

Authorization is herewith given to charge any fees or any shortages in any fees required during prosecution of this application and not paid by other means to Patent and Trademark Office deposit account 50-1199.

Respectfully submitted on Oktober 23, 2008,

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